

ABSTRACT

Proteins in the IKK and JNK signaling pathways, such as NF κ B, are involved in
5 the regulation of inflammatory diseases. Through phosphorylation and
polyubiquitination, I κ B proteins which sequester NF κ B in the cytoplasm, are degraded
by the ubiquitin-proteasome pathway releasing NF κ B to the nucleus where it is activated.
The present invention provides methods utilizing the composition of proteins in the IKK,
JNK and ubiquitin-proteasome pathways such as, TRAF6 or TRAF2 (E3-ubiquitin
10 protein ligase), TRIKA1/Uev1A/Ubc13 complex (E2-ubiquitin conjugating enzyme), and
TRIKA2/TAK1 (protein kinase), in screening for candidate modulators involved in
activation of the IKK and JNK pathways. The application further provides methods of
utilizing the candidate modulators as drug therapeutics against inflammatory and immune
diseases.